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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/829,388	04/22/2004	Edmund A. Rossi	330261	5415

35657 7590 04/30/2007

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/829,388	ROSSI ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-120* is/are pending in the application.

4a) Of the above claim(s) *5, 8-12 and 21-116* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-7, 13-20 and 117-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 April 2004 and 13 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/5/06; 9/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment filed 13 September 2004 has been entered in full.

Election/Restrictions

2. Applicant's election with traverse of the invention of Group 2, claims 1-4, 6-7, 13-20 and newly added claims 117-120 drawn to the tumor antigen CEA in the reply filed on 16 February 2007 is acknowledged. Applicant is reminded that a generic linking claim is inclusive to the linked Groups of Inventions and fully examined upon election of one of the linked Groups. The traversal is on the grounds that there are generic claims (i.e., claims 1-4, 6-7 and 13-16) covering each of the required elections and are generic to all of the claims to species in excess of one species are written in dependent form and depend from the generic claims. This has been fully considered but is not found persuasive in view the present application does not include an allowable generic to all the claimed species (e.g., see rejections set forth below). For reasons set forth in the restriction requirement mailed 16 January 2007, the inventions of Groups 2-46 are distinct and a serious search and examination burden is placed on the examiner if restriction is not required as evidenced by their different field of search and separate status in the art. See MPEP 803. Further, in view of applicants remarks and to clarify the record, the restriction among Groups 2-46 is not a species election.

Applicants request for rejoinder is acknowledged, however at this time the claimed polyvalent protein complexes are not in condition for allowance. Applicants' attention is directed to MPEP 821.04.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 5, 8-12 and 21-116 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

4. Claims 1-4, 6-7, 13-20 and 117-120 are under consideration.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on 05 January 2006 and 18 September 2006 have been fully considered by the examiner. A signed and initialed copy of each IDS is included with the instant Office Action.

Specification

6. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

7. Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Base claim 4 from which claim 6 depends recites "wherein at least two of said antigen binding sites have the same binding specificity". Thus, the recitation "wherein said antigen binding sites have the same binding specificity" does not add a limitation and as such does not further limit the claimed subject matter.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 19-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 19-20 are vague and indefinite in the recitation of "BS14HP" and "hBS14" as the sole means of identifying the polyvalent protein complex referred

to in claim 19. The use of laboratory designations to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. Further, it is unclear what if any differences exist between "BS14HP" and "hBS14". This rejection can be overcome by amending the claims to specifically and uniquely identify "BS14HP" and "hBS14", for example, by SEQ ID number.

b. Claim 6 recites the limitation "said antigen binding sites". There is insufficient antecedent basis for this limitation in the claim. Base claim 4 recites "at least two of said antigen binding sites", making it unclear if the limitation "said antigen binding sites" is referring to the two antigen binding sites or more than two antigen binding sites, i.e., "at least two antigen binding sites".

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-4, 6-7, 13-18 and 117-120 are rejected under 35 U.S.C. 102(e) as being anticipated by Rossi et al (US 2003/0162709 A1, 12/26/2001, IDS reference A02 filed 1/5/06).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application

and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to a polyvalent protein complex comprising a first and second polypeptide chain, wherein said first polypeptide chain comprises three immunoglobulin variable domains separated by two peptide linkers (i.e., V1-linker-V2-linker-V3) and wherein said second polypeptide chain comprises three immunoglobulin variable domains separated by two peptide linkers and which are arranged in the reverse order to the first polypeptide chain (i.e., V3-linker-V2-linker-V1), wherein said first and second polypeptide chains together form a complex comprising at least three antigen binding sites formed by VH-VL pairs from said first and second polypeptide chains (i.e., no VH-VL pairs from the same polypeptide chain), wherein two of the antigen binding sites are specific for CEA and wherein the third antigen binding site is specific for a hapten, including HSG of a targetable construct linked to at least one therapeutic or diagnostic agent, wherein the therapeutic agent is a drug, toxin, cytokine, lymphokine, enzyme, growth factor, radionuclide, hormone, oligonucleotide, antisense oligonucleotide, cytotoxic agent or chemotherapeutic agent and wherein the diagnostic agent is a radionuclide, a contrast agent, a dye, a fluorescent agent, a chemiluminescent agent, an enzyme, a paramagnetic ion, or an ultrasound enhancing agent and wherein each of said first or second polypeptide of the polyvalent protein complex further comprises at least 1-3 additional immunoglobulin variable domains such that the first and second polypeptides together form 4-6 antigen binding sites formed by VH-VL pairs from said first and second polypeptide chains and wherein at least one polypeptide chain further comprises an amino acid sequence selected from a toxin, a cytokine, a lymphokine, an enzyme, a growth factor and an affinity purification tag.

Rossi et al teach a multivalent, multi-specific binding protein (i.e., "polyvalent protein complex") comprising two heterologous polypeptide chains (i.e., two scFvs) associated noncovalently to from three antigen binding sites, two of which have affinity for the tumor associated antigen CEA and one hapten or

HSG binding site, wherein one of the polypeptide chains (i.e., one scFv) contains two VH domains from one antibody connected to the VL domain of a second antibody and the second polypeptide chain (i.e., second scFv) contains two VL domains from the first antibody and the VH domain of the other antibody, or one of the polypeptide chains consists of three VH domains each from an antibody of different specificity joined by peptide linkers and the second polypeptide chain consists of complementary VL domains joined by peptide linkers such that the VH and VL domains on said first and second polypeptide chains associate in an anti-parallel fashion and the two polypeptide chains may comprise more variable domains to increase the valency or the number of specificities, i.e., a tetravalent bispecific dimer that is bivalent for each of the two specificities (see entire document, particularly pp. 3-4, Example 4 and claims). Rossi et al also teach use of six histidine residues added to one of the polypeptide chains for purification by IMAC and the use of the multivalent, multi-specific binding proteins for pre-targeting CEA positive tumors for subsequent delivery of diagnostic or therapeutic agents carried by a carrier molecule comprising one or more haptens (i.e., HSG) (i.e., capable of binding simultaneously to a second polyvalent protein complex), wherein the diagnostic and therapeutic agents include isotopes, drugs, toxins, cytokines, hormones, growth factors, conjugates, radionuclides (see pp. 5-6).

Thus, Rossi et al anticipate the claims.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Byers et al (The Journal of Immunology, 140(11):4050-4055, June 1, 1988) in view of Goel et al (Cancer Research, 60:6964-6971, December 15, 2000).

The claims are drawn to a polyvalent protein complex comprising a first and second polypeptide chain, wherein said first polypeptide chain comprises three immunoglobulin variable domains separated by two peptide linkers (i.e., V1-linker-V2-linker-V3) and wherein said second polypeptide chain comprises three immunoglobulin variable domains separated by two peptide linkers and which are arranged in the reverse order to the first polypeptide chain (i.e., V3-linker-V2-linker-V1), wherein said first and second polypeptide chains together form a complex comprising at least three antigen binding sites formed by VH-VL pairs from said first and second polypeptide chains (i.e., no VH-VL pairs from the

same polypeptide chain) and each polypeptide chain may comprise an additional 1-3 variable domains to produce 4-6 antigen binding sites, wherein the antigen binding sites have the same antigen binding specificity and wherein at least one polypeptide chain is further comprises an amino acid sequence selected from the group consisting of a toxin, a cytokine, a lymphokine, a enzyme, a growth factor, and an affinity tag.

Byers et al teach a CEA specific ricin A-chain immmunotoxin that is specifically cytotoxic to CEA expressing tumors and enhanced antibody affinity leads to increased endocytosis of bound immunoconjugate and potentiates cytotoxicity (see entire document, particularly pp. 4051-4053). Byers et al do not specifically teach a CEA specific tetravalent scFv dimer (i.e., $[sc(Fv)_2]_2$) comprising two polypeptide chains each comprising four immunoglobulin variable domains that non-covalently associate to form four antigen-binding sites. This deficiency is made up for in the teachings of Goel et al.

Goel et al teach a tetravalent scFv dimer (i.e., $[sc(Fv)_2]_2$) comprising two polypeptide chains each comprising four immunoglobulin variable domains that non-covalently associate to form four antigen-binding sites and compared to divalent IgG and scFv, the tetravalent scFv dimer increased functional affinity, showed higher tumor accretion with low uptake by normal organs, which make it an important reagent for cancer therapy (see entire document, particularly abstract, Fig. 1, pp. 6967-6969).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a CEA specific tetravalent scFv dimer conjugated to ricin A chain (i.e., CEA-$[sc(Fv)_2]_2$-ricin) for therapeutic benefit in CEA positive cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to produce a CEA specific tetravalent scFv dimer conjugated to ricin A chain (i.e., CEA-$[sc(Fv)_2]_2$-ricin) for therapeutic benefit in CEA positive cancer patients in view of Byers et al and Goel et al because Byers et al teach a CEA specific ricin

A-chain immmunotoxin that is specifically cytotoxic to CEA expressing tumors and enhanced antibody affinity leads to increased endocytosis of bound immunoconjugate and potentiates cytotoxicity and Goel et al teach a tetravalent scFv dimer (i.e., $[sc(Fv)_2]_2$) comprising two polypeptide chains each comprising four immunoglobulin variable domains that non-covalently associate to form four antigen-binding sites, which increased functional affinity and showed higher tumor accretion with low uptake by normal organs compared to divalent IgG and scFv making it an important reagent for cancer therapy. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to produce a CEA specific tetravalent scFv dimer-ricin conjugate (i.e., CEA-$[sc(Fv)_2]_2$-ricin) comprising two polypeptide chains each comprising four immunoglobulin variable domains that non-covalently associate to form four antigen-binding sites, thereby increasing antibody affinity, leading to increased endocytosis and potentiating cytotoxicity of bound CEA-$[sc(Fv)_2]_2$-ricin in CEA expressing cancers. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Semaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it would have been *prima facie* obvious at the time the invention was made to produce a CEA specific tetravalent scFv dimer conjugated to ricin A chain (i.e., CEA-$[sc(Fv)_2]_2$-ricin) for therapeutic benefit in CEA positive cancer patients in view of Byers et al and Goel et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

14. Claims 1-2, 4, 6-7, 13-18 and 117-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet et al (U.S. Patent 5,256,395, 10/26/1993) in view of Karacay et al (Bioconjugate Chemistry, 77:842-854, 2000)

and Goel et al (Cancer Research, 60:6964-6971, December 15, 2000) and Hillairet de Boisferon et al (Bioconjugate Chemistry, 11(4):452-460, July-August 2000).

The claims have been described supra.

Barbet et al teach a multivalent, multi-specific binding protein comprising two or more binding sites, wherein at least one binding site has affinity towards a hapten moiety and two binding sites having affinity towards a target antigen (see Figures 2-3) and a divalent hapten linked to a diagnostic agent (i.e., radionuclide), or therapeutic agent (i.e., drugs, toxins, ect) positioned to permit simultaneous binding of said hapten moieties with said binding protein (see entire document, particularly Figures 1-3, cols. 4-5, 7-9). Barbet et al do not specifically teach wherein the multivalent, multi-specific binding protein is a CEA specific tetravalent scFv dimer (CEA-[sc(Fv)$_2$]$_2$) or wherein the hapten is HSG. These deficiencies are made up for in the teachings of Hillairet de Boisferon et al and Goel et al.

Karacay et al teach a pretargeting approach for detection and therapy of CEA expressing cancers comprising administering a bispecific antibody that comprises a CEA specific antibody fragment and an antibody fragment that binds a subsequently administered divalent hapten linked to a diagnostic or therapeutic agent and Karcay et al suggests that the use of a bispecific antibody comprising a divalent anti-CEA combined with a divalent anti-CEA combined either with a monovalent or divalent anti-hapten antibody is of interest for increasing absolute tumor uptake (see entire document, particularly pp. 849-852, pg. 852, 2nd col.)

Goel et al have been described supra.

Hillairet de Boisferon et al teach a bispecific antibody comprising a binding site that recognizes HSG (see abstract). Hillairet de Boisferon et al teach the HSG hapten has low toxicity, high affinity to available antibodies and no cross-reactivity or non-specific binding to body components (see bridging paragraph of pages 457-458 and page 458, right column).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a CEA specific tetravalent scFv dimer (i.e., CEA-$[sc(Fv)_2]_2$ that binds a divalent HSG carrier molecule comprising a diagnostic or therapeutic agent for therapeutic benefit in CEA positive cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a CEA specific tetravalent scFv dimer (i.e., CEA-$[sc(Fv)_2]_2$ that binds a divalent HSG carrier molecule comprising a diagnostic or therapeutic agent for therapeutic benefit in CEA positive cancer patients in view of Barbet et al and Karacay et al and Goel et al and Hillairet de Boisferon et al because Barbet et al multivalent, multi-specific binding protein comprising two or more binding sites, wherein at least one binding site has affinity towards a hapten moiety and two binding sites having affinity towards a target antigen (see Figures 2-3) and a divalent hapten linked to a diagnostic agent (i.e., radionuclide), or therapeutic agent (i.e., drugs, toxins, ect) positioned to permit simultaneous binding of said hapten moieties with said binding protein and Karacay et al teach a pretargeting approach for detection and therapy of CEA expressing cancers comprising administering a bispecific antibody that comprises a CEA specific antibody fragment and an antibody fragment that binds a subsequently administered divalent hapten linked to a diagnostic or therapeutic agent and Karcay et al suggests that the use of a bispecific antibody comprising a divalent anti-CEA combined with a divalent anti-CEA combined with either a monovalent or divalent anti-hapten antibody is of interest for increasing absolute tumor uptake and Goel et al teach a tetravalent scFv dimer (i.e., $[sc(Fv)_2]_2$) comprising two polypeptide chains each comprising four immunoglobulin variable domains that non-covalently associate to form four antigen-binding sites and having favorable pharmacokinetics for therapy and Hillairet de Boisferon et al teach a bispecific antibody comprising a binding site having affinity for the HSG hapten and the HSG hapten is suitable to carry radioactive isotopes to tumor cells, has low

toxicity, high affinity to available antibodies (i.e., anti-HSG antibodies) and no cross-reactivity or non-specific binding to body components. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated by then goal of increasing the functional affinity and the amount of bispecific antibody localized at the tumor site in the pretargeting method of Barbet and Karacay by producing a CEA specific tetravalent scFv dimer (i.e., CEA-$[sc(Fv)_2]_2$ comprising at least two binding sites for CEA and a binding site for a subsequently administered diavalent hapten-diagnostic/therapeutic agent according to the pretargeting method of Barbet and Karacay for increased absolute tumor uptake of the diagnostic or therapeutic agent. Further, one of ordinary skill in the art would have been motivated to use the HSG hapten as the carrier molecule for the diagnostic and therapeutic agents as taught by Barbet because HSG has low toxicity, high affinity to available antibodies and no-cross reactivity or non-specific binding to body components. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a CEA specific tetravalent scFv dimer (i.e., CEA-$[sc(Fv)_2]_2$ that binds a divalent HSG carrier molecule comprising a diagnostic or therapeutic agent for therapeutic benefit in CEA positive cancer patients in view of Barbet et al and Karacay et al and Goel et al and Hillairet de Boisferon et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Cochlovius et al. Cancer Research, 60:4336-4341, August 15, 2000. Cochlovius et al teach bispecific tetravalent scFv dimers, which is relevant to the structure of the polyvalent protein complexes claimed in the instant application.

Nakamura et al. Cancer, 80(12 Suppl):2650-2655, December 15, 1997.

Nakamura teach a CEA specific monoclonal antibody conjugated to IL-2 specifically enhanced tumor vascular permeability and that augmented tumor uptake, which is relevant to the claimed polyvalent protein complexes further comprising a cytokine.

Bhatia et al. International Journal of Cancer, 85:571-577, 2000.

Bhatia et al teach a CEA specific antibody fused to the enzyme carboxypeptidase G2 for antibody-directed enzyme prodrug therapy (ADEPT), which is relevant to the claimed polyvalent protein complexes further comprising an enzyme.

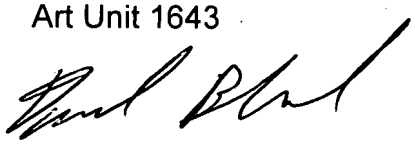
16. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Blanchard
Patent Examiner
Art Unit 1643



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April 27, 2007